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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/758,575	01/09/2001	Joerg Kaufmann	59516-216/pp-01656.002	9437

7590 08/28/2007

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EXAMINER	
HARRIS, ALANA M	
ART UNIT	**PAPER NUMBER**
1643	

MAIL DATE	DELIVERY MODE
08/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/758,575	KAUFMANN ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-11 and 36-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1 and 6-11* is/are allowed.

6)☒ Claim(s) *5, 36-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/07/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments and Amendments

1. Claims 1, 5-11 and 36-48 are pending.

Claims 39 and 45-47 have been amended.

Claim 48 has been added.

Claims 1, 5-11 and 36-48 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections

Claim Objections

3. The objection of claims 39, 45 and 46 because of the informalities cited in the Action mailed March 8, 2007 have been withdrawn in light of Applicants' amendment to claim 39 and arguments presented in regard to claims 45 and 46.

Withdrawn Rejection

Claim Rejections - 35 USC § 112

4. The rejection of claims 45-47 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn.

New Grounds of Objection

Claim Objections

5. Claim 46 is objected to because of the following informality: the word "the" is cited twice in line 2. Correction is required.

New Grounds of Rejections and Maintained Rejections

Claim Rejections - 35 USC § 112

6. The **NEW MATTER REJECTION** of claim 47 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained.

Applicants direct the Examiner's attention to page 22, lines 22 and 23 in order to clarify the issue of support for the recitation "nucleotides 46-1173". Via a telephone conversation with Applicants' representative, Mr. Gwilym J.O. Attwell on Tuesday, August 14, 2007 the Examiner noted the said page lists "446" and not "46". Until the claim is amended to recite what is noted in the specification the rejection is maintained.

7. Claim 48 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.**

Claim 48 has been added to the claim set with the submission of the Remarks, filed May 31, 2007. Applicants allege support for this claim is found in the pages and

lines set forth on page 6 of the Remarks, see 3rd paragraph. The Examiner has reviewed the specification and the specific sites listed by Applicants and does not note support for the isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide; a polynucleotide at least 95% identical to a polynucleotide; and a polynucleotide encoding a polypeptide at least 95% identical to SEQ ID NO: 2 wherein the nucleic acid molecule comprises nucleotides 365-1173 of SEQ ID NO: 1. One particular citation on page 23, lines 13-16 states "[t]he antisense sequence is complementary to at least a portion of the coding sequence (nucleotides 365-1173) of a metastatic marker gene having a nucleotide sequence shown in SEQ ID NO: 1." The context of this recitation does not overlap with the claimed invention. In essence, this passage within the specification does not support the breadth of the claims and further more it seems nucleotides 365-1173 of SEQ ID NO: 1 do not encode amino acids 1 to 273; amino acids 2 to 273; nor 26 to 273 of SEQ ID NO: 2. Applicants should delete the new matter or point out support for claim 48.

8. Claims 5 and 36-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants broadly claim an isolated nucleic acid molecule that is at least 95%-98% identical to polynucleotides encoding amino acids; and

an isolated nucleic acid molecule comprising polynucleotide encoding a polypeptide with no more than 5 conservative amino acid substitutions;

wherein the amino acids/polypeptide has the amino acid sequence selected from the group consisting of:

1 to 273 of SEQ ID NO: 2;

2 to 273 of SEQ ID NO: 2; and

26 to 273 of SEQ ID NO: 2. The said polynucleotide is contained in vector and host cell and produced utilizing art known recombinant technology. The written description in this instant case only sets forth wild type hsOAF (polynucleotide, SEQ ID NO: 1, which encodes polypeptide, SEQ ID NO: 2 in its entirety) and not molecules sharing less than 100% sequence identity to the said sequences. The written description is not commensurate in scope with claims drawn to variants of SEQ ID NO: 1 and SEQ ID NO: 2, which have not been defined by functional or structural characteristics.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

With the exception of wild-type hsOAF (SEQ ID NO: 1 and SEQ ID NO: 2), the skilled artisan cannot envision the detailed structure or function of the encompassed polypeptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Likewise, the skilled artisan cannot envision the detailed structure or function of nucleic acids that share less than 100% sequence identity to SEQ ID NO: 1 and their encoded products. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The polypeptides and molecules germane to the methodology itself are required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement, which defines a genus of nucleic acids by only their functional activity, does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

At the time the application was filed Applicants only had possession of nucleic acids that encode SEQ ID NO: 2 and not nucleic acid sequences that encode

polypeptides with reduced sequence homology that may or may not act in the manner suggested by the specification. The specification does not evidence the possession of nucleic acid molecules that may or may not encode hsOAF molecules. Nor does the specification teach any polynucleotides with 95-98% sequence identity and those molecules, which encode a polypeptide having conservative amino acid substitutions. There is insufficient support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

The full breadth of the claims does not meet the written description provision of 35 U.S.C. 112, first paragraph.

9. Claims 5 and 36-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants broadly claim an isolated nucleic acid molecule that is at least 95%-98% identical to polynucleotides encoding amino acids; and

an isolated nucleic acid molecule comprising polynucleotide encoding a polypeptide with no more than 5 conservative amino acid substitutions;

wherein the amino acids/polypeptide has the amino acid sequence selected from the group consisting of:

1 to 273 of SEQ ID NO: 2;

2 to 273 of SEQ ID NO: 2; and

26 to 273 of SEQ ID NO: 2. The said polynucleotide is contained in vector and host cell and produced utilizing art known recombinant technology. The specification while being enabling for the nucleic acid identified as SEQ ID NO: 1 which encodes the amino acid sequence, SEQ ID NO: 2, does not reasonably provide enablement for variants that have at least 95% sequence identity to polynucleotides that encode SEQ ID NO: 2. Furthermore, nucleic acids that encode polypeptides with substitutions placed inside a vector and consequently a host cell would not encode a protein or the protein of SEQ ID NO: 2. There is no guidance as to how to use these divergent sequences.

The encoded products of these at least 95% sequence identical nucleic acids may possess function that is not commensurate with the functions of the native protein. The nucleic acids will encode proteins that may not maintain the activities proposed in the specification, such as a marker for distinguishing between tumors, which will or have metastasized. Likewise, it would seem that specific function(s) would be required to make the encoded protein useful for the applications disclosed in the specification and the claims. Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acid or acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved and detailed knowledge of

the ways in which the protein's structure relates to its function. The specification provides essentially no guidance as to which of the infinite possible choices is likely to be successful especially in selection of at least one conservative amino acid substitution within the range *of about 1 to about 273 amino acid residues of SEQ ID NO: 2* (see claim 5). The true fact of the state of the art in peptide chemistry is expressed succinctly in the accompanying Lazar article (Molecular and Cellular Biology 8(3): 1247-1252, March 1988). This article presents data that substantiates the fact that the introduction of mutations in an amino acid sequence will yield products with different biological activity from the wild type protein.

From the discussion above, it is clear that the predictability of changes to the nucleic acid sequence and its forthcoming amino acid sequence is practically nil as far as biological activities are concerned. Moreover, a sequence(s) that encodes a protein with substitutions is more than likely to result in expression of polypeptide inconsistent with SEQ ID NO: 2. The specification fails to provide sufficient guidance to enable one of ordinary skill in the art to make and use the claimed nucleic acids in a manner reasonably correlated with the broad scope of the claims. Without such guidance, the changes which must be made in the nucleic acid sequence of SEQ ID NO: 1, which results in nucleic acid sequences with 95% identity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.,* 18 USPQ2d 1016 and *Ex parte Forman,* 230 USPQ 546 (BPAI 1986).

Allowable Subject Matter

10. Claims 1 and 6-11 are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner works a flexible schedule, however she can normally be reached between the hours of 7:30 am to 6:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
22 August 2007